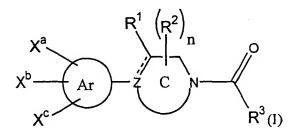
## WHAT IS CLAIMED IS:

## 1. A compound of compound of formula I:



5 wherein:

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Z is a carbon or nitrogen atom;

is a 4 to 7-membered azaheterocyclyl or a 4 to 7-membered azaheterocyclenyl group;
is a single or double bond, provided that when Z is a nitrogen atom, then is a single bond;

is an aryl group, a monocyclic heteroaryl group, or a bicyclic azaheteroaryl group

which includes a first proximal ring that is attached to the moiety and a ring distal to said first ring, said distal ring including at least one nitrogen atom;

R1 is hydrogen, -CH2OR12, -CH2SR12, -CO2R13, -C(O)R13, or -CONR13R13;

R2 is hydrogen, alkyl, aralkyl, aralkenyl, aralkynyl, heteroaralkyl, heteroaralkenyl, heteroaralkynyl, hydroxy, hydroxyalkyl, alkoxy, aryloxy, aralkoxy, acyl, aroyl, halo, nitro, cyano, carboxy, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, alkylsulfonyl, arylsulfonyl, heteroarylsulfonyl, alkylsulfonyl, arylsulfinyl, heteroarylsulfinyl, alkylthio, arylthio, heteroarylthio, aralkylthio, heteroaralkylthio, Y1Y2N-, Y1Y2N-alkyl-, Y1Y2NCO- or Y1Y2NSO2-;

R<sup>3</sup> is cycloalkyl, cycloalkenyl, heterocyclyl, heterocyclenyl, fused arylcycloalkyl, fused heteroarylcycloalkyl, fused arylcycloalkenyl, fused heteroarylcycloalkenyl, fused arylheterocyclyl, fused heteroarylheterocyclyl, fused arylheterocyclyl, fused

heteroarylheterocyclenyl, aryl, fused cycloalkenylaryl, fused cycloalkylaryl, fused heterocyclylaryl, fused heterocyclenylaryl, heteroaryl, fused cycloalkylheteroaryl, fused cycloalkenylheteroaryl, fused heterocyclenylheteroaryl, fused heterocyclylheteroaryl; Xa, Xb, Xc are independently selected from hydrogen, R<sup>4</sup>R<sup>5</sup>N-, (hydroxy)HN-, (alkoxy)HN-,

5 R<sup>6</sup>O-, R<sup>4</sup>R<sup>5</sup>NCO-, R<sup>4</sup>R<sup>5</sup>NSO<sub>2</sub>-, R<sup>6</sup>CO-, halo, cyano, nitro R<sup>7</sup>(O)C(CH<sub>2</sub>)<sub>q</sub>- and H<sub>2</sub>N

and when is a bicyclic heteroaryl group, then Xc is a substituent that is at the alpha

position with respect to a nitrogen atom of said distal ring of and Xc is selected from the group consisting of H, hydroxy and H<sub>2</sub>N-, (optionally substituted lower alkyl)HN (hydroxy)HN-, and (alkoxy)HN-;

10 R<sup>4</sup> and R<sup>5</sup> are independently H or optionally substituted lower alkyl, or one of R<sup>4</sup> and R<sup>5</sup> is H and the other of R<sup>4</sup> and R<sup>5</sup> is R<sup>7</sup>(O)CCH<sub>2</sub>- or lower acyl;

R<sup>6</sup> is H, optionally substituted lower alkyl, lower acyl or R<sup>7</sup>(O)CCH<sub>2</sub>-;

R<sup>7</sup> is H, optionally substituted lower alkyl, alkoxy or hydroxy;

 $R^8$  and  $R^9$  taken together are =NR<sup>10</sup>;

15 R<sup>10</sup> is hydrogen, R<sup>11</sup>O<sub>2</sub>C-, R<sup>11</sup>O-, HO-, cyano, R<sup>11</sup>CO-, HCO-, lower alkyl, nitro, or γ<sup>1</sup>aγ<sup>2</sup>a<sub>N-</sub>;

R<sup>11</sup> is alkyl, aralkyl, or heteroaralkyl;

R<sup>12</sup> is hydrogen, lower alkyl, aryl(lower alkyl), heteroaryl(lower alkyl), lower acyl, aroyl, or heteraroyl;

20 R<sup>13</sup> is hydrogen, lower alkyl;

 $Y^1$  and  $Y^2$  are independently hydrogen, alkyl, aryl, and aralkyl, or where the substituent is  $Y^1Y^2N$ - or  $Y^1Y^2N$ -alkyl- then one of  $Y^1$  and  $Y^2$  is acyl or aroyl and the other of  $Y^1$  and  $Y^2$  is hydrogen, alkyl, aryl, or aralkyl;

Y<sup>1a</sup> and Y<sup>2a</sup> are independently hydrogen or alkyl;

25 n is 1, 2, 3, or 4; or

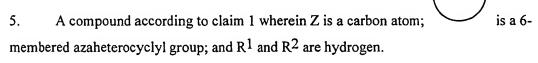
a pharmaceutically acceptable salt thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

2. A compound according to claim 1 wherein Z is a carbon atom.

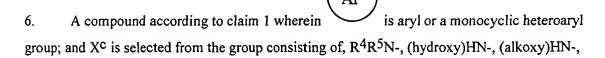
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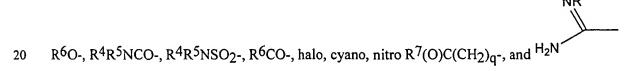
3. A compound according to claim 1 wherein Z is a carbon atom; is a 6-membered azaheterocyclyl or a 6-membered azaheterocyclenyl group; R<sup>1</sup> is selected from the group consisting of hydrogen -CH<sub>2</sub>OR<sup>12</sup>, -CH<sub>2</sub>SR<sup>12</sup>, -CO<sub>2</sub>R<sup>13</sup>, -C(O)R<sup>13</sup> and -CONR<sup>13</sup>R<sup>13</sup>; R<sup>12</sup> is hydrogen, lower alkyl, aryl(lower alkyl), or heteroaryl(lower alkyl); and R<sup>13</sup> is hydrogen, or lower alkyl.

4. A compound according to claim 1 wherein Z is a carbon atom; is a 6-membered azaheterocyclenyl group; is a double bond; and R<sup>1</sup> and R<sup>2</sup> are hydrogen.



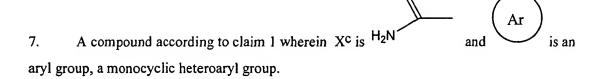
A compound according to claim 1 wherein R<sup>3</sup> is optionally substituted (phenyl substituted phenyl), optionally substituted (heteroaryl substituted phenyl), optionally substituted (phenyl substituted heteroaryl) or optionally substituted (heteroaryl substituted heteroaryl).





NR<sup>10</sup>

NR<sup>10</sup>



- 8. A compound according to claim 1 wherein X<sup>c</sup> is H<sub>2</sub>N and is in the meta position with respect to the to the position of attachment of the moiety to the
- Z C N moiety.

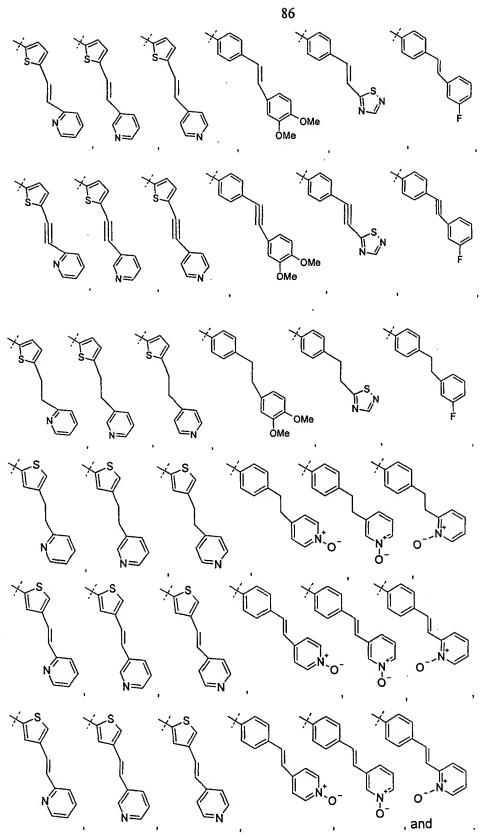
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9. A compound according to claim 1 wherein is a bicyclic azaheteroaryl group which includes a first proximal ring that is attached to the moiety and a ring distal to said first ring; X<sup>c</sup> is R<sup>4</sup>R<sup>5</sup>N-, (hydroxy)HN-, or (alkoxy)HN-, and X<sup>c</sup> is in the alpha position with respect to a nitrogen atom in said distal ring.

10. A compound according to claim 1, which is selected from the group consisting of

wherein R³ is selected from the group consisting of



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11.
             A compound according to claim 1 selected from the group consisting of
     3-{1-[4-(6-Oxo-1,6-dihydropyridine-3-yl)-benzoyl]-1,2,3,6-tetrahydropyridin-4 yl}benzamidine;
     3-{1-[4-(1-Oxypyridin-2-yl)-benzoyl]-1,2,3,6-tetrahydropyridin-4 yl}benzamidine;
     3-{1-[4-(1-Oxypyridin-4-yl)-benzoyl]-1,2,3,6-tetrahydropyridin-4-yl}benzamidine;
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     3-{1-[4-(6-Oxo-1,6-dihydropyridine-3-yl)-benzoyl]-piperidin-4-yl} benzamidine;
     3-{1-[4-(1-Oxypyridin-4-yl)-benzoyl]-piperidin-4-yl}benzamidine;
     3-{1-[4-(1-Oxypyridin-2-yl)-benzoyl]-piperidin-4-yl} benzamidine;
     3-[1-(4-Pyridine-2-yl-benzoyl)-1,2,3,6-tetrahydropyridin-4-yl]benzamidine;
      3-[1-(4-Pyridin-3-yl-benzoyl)-1,2,3,6-tetrahydropyridin-4-yl]benzamidine;
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     3-[1-(4-Pyridin-4-yl-benzoyl)-1,2,3,6-tetrahydropyridin-4-yl]benzamidine;
      3-{1-[4-(5-Bromofuran-2-yl)-benzoyl]-1,2,3,6-tetrahydropyridin-4-yl}benzamidine;
      3-{1-[4-(5-Chlorothiophen-2-yl)-benzoyl]-1,2,3,6-tetrahydropyridin-4-yl} benzamidine;
      3-{1-(4-Thiophen-2-yl-benzoyl)-1,2,3,6-tetrahydropyridin-4-yl}benzamidine;
      3-{1-[3-(5-Chlorothiophen-2-yl)-acryloyl)-1,2,3,6-tetrahydropyridin-4-yl}benzamidine;
      3-[1-(4-{2-[(2-Dimethylaminoethyl)methylamino]pyrimidin-4-yl}benzoyl)-1,2,3,6-
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      tetrahydropyridin-4-yl}benzamidine;
      3-(1-{4-[2-(2-Dimethylaminoethyl)-6-oxo-1,6-dihydropyridin-3-yl]benzoyl}-1,2,3,6-
      tetrahydropyridin-4-yl)benzamidine;
      3-[1-(4-Pyrimidin-2-ylbenzoyl)-1,2,3,6-tetrahydropyridin-4-yl]-benzamidine;
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      3-[1-(4-Pyrazin-2-ylbenzoyl)-1,2,3,6-tetrahydropyridin-4-yl]-benzamidine;
      3-[1-(4'-Sulfamoylbiphenyl-4-carbonyl)-1,2,3,6-tetrahydropyridin-4-yl]-benzamidine;
      3-[1-(3'-Sulfamoylbiphenyl-4-carbonyl)-1,2,3,6-tetrahydropyridin-4-yl]-benzamidine;
      3-{1-[4-(6-Methoxypyridazin-3-yl)benzoyl]-1,2,3,6-tetrahydropyridin-4-yl]-benzamidine;
      3-{1-[4-(6-Oxo-1,6 dihydropyridazin-3-yl)benzoyl]-1,2,3,6-tetrahydropyridin-4-yl]-benzamidine;
      3-{1-[4-(2-Aminopyrimidin-5-yl)benzoyl]-1,2,3,6-tetrahydropyridin-4-yl]-benzamidine;
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      3-{1-[4-(6-Methoxypyridin-3-yl)benzoyl]-1,2,3,6-tetrahydropyridin-4-yl]-benzamidine;
      3-[1-(4-(Pyrimidin-5-ylbenzoyl)-1,2,3,6-tetrahydropyridin-4-yl]-benzamidine;
      3-[1-(4-Pyridin-2-ylbenzoyl)-piperidin-4-yl]benzamidine;
      3-[1-(4-Pyridin-3-ylbenzoyl)-piperidin-4-yl]benzamidine;
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      3-[1-(4-Pyridin-4-ylbenzoyl)-piperidin-4-yl]benzamidine;
      3-{1-[4-(6-Methoxypyridin-3-yl)benzoyl]-piperidin-4-yl}benzamidine;
      3-{1-[4-(6-Methoxypyridazin-3-yl)benzoyl]-piperidin-4-yl}benzamidine;
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- 3-{1-[4-(6-Oxo-1,6-dihydropyridazin-3-yl)benzoyl]-piperidin-4-yl}benzamidine;
- 5-{4-[4-(1-Aminoisoquinolin-7-yl)piperidine-1-carbonyl]phenyl}-1H-pyridin-2-one;
- 5-[4-(1-Aminoisoquinolin-7-yl)piperidine-1-carbonyl]-1'H-[2,3']bipyridinyl-6'-one;
- [4-(1-Aminoisoquinolin-7-yl)piperidin-1-yl][2-fluoro-4-(6-methoxypyridin-3-
- 5 yl)phenyl]methanone;
  - [4-(1-Aminoisoquinolin-7-yl)piperidin-1-yl](2-fluoro-4-pyridin-3-ylphenyl)methanone;
  - 4'-[4-(1-Aminoisoquinolin-7-yl)piperidine-1-carbonyl]biphenyl-3-carboxylic acid amide;
  - [4-(1-Aminoisoquinolin-7-yl)piperidin-1-yl][5-(6-methoxypyridin-3-yl)thiophen-2-yl]]methanone;
- 5-{4-[4-(1-Aminoisoquinolin-7-yl)piperidine-1-carbonyl]-3-fluorophenyl}-1H-pyridin-2-one;
  - 5-{5-[4-(1-Aminoisoquinolin-7-yl)piperidine-1-carbonyl]thiophen-2-yl}-1H-pyridin-2-one;
  - 5-{4-[4-(1-Aminoisoquinolin-7-yl)-3,6-dihydro-2H-pyridine-1-carbonyl]phenyl}-1H-pyridin-2-one:
  - [4-(1-Aminoisoquinolin-7-v1)-3,6-dihydro-2H-pyridin-1-yl](4-pyridin-4-ylphenyl)methanone;
- 15 [4-(1-Aminoisoquinolin-7-yl)piperidin-1-yl][4-(6-methoxypyridin-3-yl)phenyl]methanone;
  - [4-(1-Aminoisoquinolin-7-yl)piperidin-1-yl](4-pyridin-3-ylphenyl)methanone;
  - [4-(1-Aminoisoquinolin-7-yl)piperidin-1-yl](6'-methoxy-[2,3']bipyridin-5-yl)methanone;
  - 5-{4-[4-(4-Amino-1H-pyrrolo[3,2-c]pyridin-2-yl)piperidine-1-carbonyl]phenyl}-1H-pyridin-2-one;
- 5-[4-(4-Amino-1H-pyrrolo[3,2-c]pyridin-2-yl)piperidine-1-carbonyl]-1'H-[2,3']bipyridinyl-6'-one;
  - 3-[1-(5-Phenylethyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzamidine;
  - 3-[1-(5-Phenylethynyl-pyridine-3-carbonyl)-1,2,3,6-tetrahydropyridin-4-yl]-benzamidine;
  - 3-[1-(5-Phenylethynyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzamidine; and
- 25 3-[4-(5-Phenylethyl-pyridine-3-carbonyl)-piperazin-1-yl]-benzamidine.

## 12. A compound according to claim 1 wherein

Z is a nitrogen atom; is a 6-membered azaheterocyclyl or a 6-membered azaheterocyclenyl group; is a single bond; and R<sup>1</sup> and R<sup>2</sup> are hydrogen.

13. A compound according to claim 1 wherein

Z is a nitrogen atom; is a 6-membered azaheterocyclyl or a 6-membered azaheterocyclenyl group; is a single bond; and R<sup>1</sup> is selected from the group consisting of hydrogen -CH<sub>2</sub>OR<sup>12</sup>, -CH<sub>2</sub>SR<sup>12</sup>, -CO<sub>2</sub>R<sup>13</sup>, -C(O)R<sup>13</sup> and -CONR<sup>13</sup>R<sup>13</sup>.

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14. A compound according to claim 12 or 13 wherein

R<sup>3</sup> is optionally substituted (phenyl substituted aralkyl), optionally substituted (heteroaryl substituted aralkyl), optionally substituted (phenyl substituted heteroaralkyl) or optionally substituted (heteroaryl substituted heteroaralkyl).

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15. A compound according to claim 12 or 13 wherein

R<sup>3</sup> is optionally substituted (phenyl substituted aralkenyl), optionally substituted (heteroaryl substituted aralkenyl), optionally substituted (phenyl substituted heteroaralkenyl) or optionally substituted (heteroaryl substituted heteroaralkenyl).

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16. A compound according to claim 12 or 13 wherein

R<sup>3</sup> is optionally substituted (phenyl substituted aralkynl), optionally substituted (heteroaryl substituted aralkynl), optionally substituted (phenyl substituted heteroaralkynl) or optionally substituted (heteroaryl substituted heteroaralkynl), (wherein the term "optionally substituted" before the term in the parenthesis, denote that the phenyl, heteroaryl, aralkynl, heteroaralkynl portions thereof could be further substituted as noted per their definitions).

- 17. A compound according to claim 1 selected from the group consisting of
- 3-[1-(5-Phenylethyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzamidine;
- 25 3-[1-(5-Phenylethynyl-pyridine-3-carbonyl)-1,2,3,6-tetrahydropyridin-4-yl]-benzamidine;
  - 3-[1-(5-Phenylethynyl-pyridine-3-carbonyl)-piperidin-4-yl]-benzamidine;
  - 3-{1-[4-(6-Methoxypyridin-3-yl)benzoyl]-1,2,3,6-tetrahydropyridin-4-yl]-benzamidine;
  - 3-[1-(4-(Pyrimidin-5-ylbenzoyl)-1,2,3,6-tetrahydropyridin-4-yl]-benzamidine;
  - 3-{1-[4-(6-Methoxypyridazin-3-yl)benzoyl]-piperidin-4-yl}benzamidine;
- 30 3-{1-[4-(1-Oxypyridin-2-yl)-benzoyl]-piperidin-4-yl} benzamidine;

- 3-[1-(4-Pyridine-2-yl-benzoyl)-1,2,3,6-tetrahydropyridin-4-yl]benzamidine;
- 3-[1-(4-Pyridin-4-yl-benzoyl)-1,2,3,6-tetrahydropyridin-4-yl]benzamidine;
- 3-[1-(4-{2-[(2-Dimethylaminoethyl)methylamino]pyrimidin-4-yl}benzoyl)-1,2,3,6-tetrahydropyridin-4-yl}benzamidine; and
- 5 3-[4-(5-Phenylethyl-pyridine-3-carbonyl)-piperazin-1-yl]-benzamidine.
  - 18. A compound according to claim 1 selected from the group consisting of
  - 3-{1-[4-(1-Oxypyridin-4-yl)-benzoyl]-1,2,3,6-tetrahydropyridin-4-yl}benzamidine;
  - 3-{1-[4-(6-Oxo-1,6-dihydropyridine-3-yl)-benzoyl]-piperidin-4-yl}benzamidine;
- 3-{1-[4-(1-Oxypyridin-4-yl)-benzoyl]-piperidin-4-yl}benzamidine;

effective amount of a compound according to claim 1 or claim 17.

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- 3-{1-[4-(6-Oxo-1,6-dihydropyridine-3-yl)-benzoyl]-1,2,3,6-tetrahydropyridin-4-yl}benzamidine;
- 3-{1-[4-(6-Oxo-1,6 dihydropyridazin-3-yl)benzoyl]-1,2,3,6-tetrahydropyridin-4-yl]-benzamidine; and
- 3-{1-[4-(6-Oxo-1,6-dihydropyridazin-3-yl)benzoyl]-piperidin-4-yl}benzamidine.
- 19. A method for treating a patient suffering from a disease state capable of being modulated by inhibiting tryptase activity comprising administering to said patient a pharmaceutically
- 20. A method for preventing and treating an inflammatory diseases associated with tryptase activity comprising administering to said patient a pharmaceutically effective amount of a compound according to claim 1 or claim 17.
- A method for preventing and treating late phase bronchoconstriction associated with
   chronic asthma comprising administering to said patient a pharmaceutically effective amount of a compound according to claim 1 or claim 17.
  - 22. A method according to claim 19 wherein said disease state is selected from the group consisting of immunomediated inflammatory disorders associated with tryptase activity, such as rheumatoid arthritis, osteoarthritis, gouty arthritis, rheumatoid spondylitis, diseases of joint cartilage destruction, ocular conjunctivitis, vernal conjunctivis, inflammatory bowel disease, asthma, allergic rhinitis, and interstitial lung diseases.

- 23. A method according to claim 19 wherein said disease state is selected from the group consisting of fibrosis, sceleroderma, pulmonary fibrosis, liver cirrhosis, myocardial fibrosis, neurofibromas, hypertrophic scars, and various dermatological conditions, for example, atopic dermatitis and psoriasis.
- A method according to claim 19 wherein said disease state is selected from the group consisting of myocardial infarction, stroke, angina and other consequences of atherosclerotic plaque rupture; as well as periodontal disease, diabetic retinopathy, tumor growth, anaphylaxis, multiple sclerosis, peptic ulcers, and syncytial viral infections.
- 25. A method of inhibiting tryptase activity comprising contacting a tryptase inhibitory amount of a compound of according to claim 1 or claim 17 with a composition containing tryptase.

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- 26. A method of treating a patient suffering from a disease state capable of being modulated by inhibiting tryptase activity comprising administering to a patient, in need thereof, a compound according to claim 1 or claim 17 or a pharmaceutically acceptable salt thereof, and optionally at least one compound selected from the group consisting of a  $\beta$ -adrenergic agonist compound, an anti-inflammatory corticosteroid compound, an anti-holinergics compound, and an anti-inflammatory compound, or a pharmaceutically acceptable salt thereof, wherein said  $\beta$ -adrenergic agonist compound is selected from the group consisting of albuterol, terbutaline, formoterol, fenoterol, and prenaline; said anti-inflammatory corticosteroid compound is selected from the group consisting of beclomethasone, triamcinolone, flurisolide, and dexamethasone; said anti-holinergics compound is ipratropium bromide; and said anti-inflammatory compound is selected from the group consisting of sodium cromoglycate and nedocromil sodium.
- 27. A pharmaceutical composition comprising a pharmaceutically acceptable amount of the compound according to claim 1 and a pharmaceutically acceptable carrier.

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- 28. A method for treating a patient suffering from a physiological condition capable of being modulated by inhibiting activity of Factor Xa comprising administering to said patient a pharmaceutically effective amount of the compound according to claim 2 or 18.
- 29. The method according to claim 28 wherein the physiological condition is venous vasculature, arterial vasculature, abnormal thrombus formation, acute myocardial infarction, unstable angina, thromboembolism, acute vessel closure associated with thrombolytic therapy, percutaneous transluminal coronary angioplasty, transient ischemic attacks, stroke, intermittent claudication or bypass grafting of the coronary or peripheral arteries, vessel luminal narrowing, restenosis post coronary or venous angioplasty, maintenance of vascular access patency in long-term hemodialysis patients, pathologic thrombus formation occurring in the veins of the lower extremities following abdominal, knee and hip surgery, a risk of pulmonary thromboembolism, or disseminated systemic intravascular coagulopathy occurring in vascular systems during septic shock, certain viral infections or cancer.

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- 30. The method according to claim 28 wherein the physiological condition is abnormal thrombus formation, acute myocardial infarction, unstable angina, thromboembolism, acute vessel closure associated with thrombolytic therapy, transient ischemic attacks, intermittent claudication or bypass grafting of the coronary or peripheral arteries, restenosis post coronary or venous angioplasty, pathologic thrombus formation occurring in the veins of the lower extremities following abdominal, knee and hip surgery or a risk of pulmonary thromboembolism.
- 31. The method according to claim 28 wherein the physiological condition is stroke, vessel luminal narrowing, maintenance of vascular access patency in long-term hemodialysis patients, or disseminated systemic intravascular coagulopathy occurring in vascular systems during septic shock, certain viral infections or cancer.
- 32. A method of inhibiting Factor Xa comprising contacting a Factor Xa inhibitory amount of a compound according to claim 2 or claim 18 with a composition containing Factor Xa.

- 33. A method of inhibiting the formation of thrombin comprising contacting Factor Xa inhibitory amount of a compound according to claim 2 or claim 18 with a composition containing Factor Xa.
- 34. A method for treating a patient suffering from a physiological condition capable of being modulated by directly inhibiting activity of both Factor Xa and Factor IIa (thrombin) comprising administering to said patient a pharmaceutically effective amount of the compound according to claim 2 or claim 18.
- 35. A method of treating a patient suffering from a disease state capable of being modulated by inhibiting Factor Xa activity comprising administering to a patient, in need thereof, a compound according to claim 2 or claim 18 or a pharmaceutically acceptable salt thereof, and optionally at least one compound selected from the group consisting of a cardioprotective agent, a direct thrombin inhibitor, an anticoagulant, an antiplatelet agent or fibrinolytic agent.